THYROID PROFILE IN CHRONIC RENAL FAILURE

Dissertation submitted to

THE TAMIL NADU
Dr.M.G.R.MEDICAL UNIVERSITY

in partial fulfillment of the regulations
for the award of the degree of

M.D. BRANCH - I
GENERAL MEDICINE

GOVT. STANLEY MEDICAL COLLEGE & HOSPITAL
THE TAMIL NADU Dr.M.G.R. MEDICAL UNIVERSITY
CHENNAI, INDIA

MARCH 2008

CERTIFICATE

This is to certify that the dissertation titled **"THYROID PROFILE IN CHRONIC RENAL FAILURE"** is the bonafide original work of **Dr.K.KARUNAKARAN,** in partial fulfillment of the requirements for **M.D.Branch – I (General Medicine)** Examination of the Tamil Nadu Dr.M.G.R Medical University to be held in March 2008. The Period of study was from September 2006 to August 2007.

Dr. MYTHILI BHASKARAN, M.D.,
D E A N
Govt. Stanley Medical College
and Hospital
Chennai – 600 001

Prof.S.NATARAJAN, M.D.,
Professor and Head
Department of Medicine
Govt. Stanley Medical College
and Hospital
Chennai 600 001

DECLARATION

I, **Dr.K.KARUNAKARAN,** solemnly declare that dissertation titled **"THYROID PROFILE IN CHRONIC RENAL FAILURE**" is a bonafide record of work done by me in the Department of Internal Medicine, Government Stanley Medical College and Hospital during September 2006 to August 2007 under the guidance of **Prof.S.NATARAJAN, M.D.,** Professor and Head Department of Medicine, Government Stanley Medical College and Hospital, Chennai.

This dissertation is submitted to Tamil Nadu Dr.M.G.R Medical University, in partial fulfillment of the University regulations for the award of M.D. Degree (Branch – I) in General Medicine – March 2008.

Place : Chennai.

Date :

(Dr.K.KARUNAKARAN)

ACKNOWLEDGEMENT

I would like to thank our beloved Dean, Govt. Stanley Medical College and Hospital, **Dr.MYTHILI BHASKARAN, M.D.,** for permitting me to utilize the hospital facilities for this dissertation.

I extend my sincere thanks to **Prof. S. NATARAJAN, M.D.,** Professor and Head of the Department of Medicine, Govt. Stanley Medical College and Hospital for his guidance during the study.

I owe my sincere thanks to my Assistant Professors **Dr.R.S.MURALIDHARAN, M.D.,** and **Dr.C.S.GOWTHAM, M.D.,** for their vlauable advice and appropriate suggestions.

I express my sincere thanks to **Dr.VIJAYAKUMAR, M.D., D.M.,** Professor of Nephrology, for permitting me to utilize the facilities in the Nephrology Ward for the purpose of this study.

Finally, I thank all the patients for their extreme patience and co-operation.

CONTENTS

ABBREVIATIONS

CKD	-	Chronic Kidney Disease
DIT	-	Diiodotyrosine
ESRD	-	End stage renal disease
FT4	-	Free Thyroxine
GFR	-	Glomerular Filtration Rate
MIT	-	Monoiodotyrosine
PTH	-	Parathyroid hormone
T3	-	Triiodothyronine
T4	-	Thyroxine
TRH	-	Thyrotropin Releasing Hormone
TSH	-	Thyroid Stimulating Hormone
TBG	-	Thyroxine Binding Globulin

INTRODUCTION

Chronic Renal Failure is a clinical syndrome due to irreversible renal dysfunction leading to excretory, metabolic and synthetic failure culminating into accumulation of non-protein nitrogenous substances and present with various clinical manifestations.

End stage renal disease is described as a terminal stage of chronic renal failure that without replacement therapy would result in death.

Despite various etiologies, CRF is the final common pathway of irreversible destruction of nephrons ultimately resulting in alteration of 'Milieu interior' that affects every system in the body. One such system in the body is thyroid hormonal system. Kidney is closely related to thyroid in the fact that it is the only other organ that competes with iodide clearance[28].

Patients with CRF have many signs and symptoms suggestive of thyroid dysfunction like sallow complexion, edema, dry skin, cold intolerance, decreased BMR, asthenia and hyporeflexia. So in cases of CRF, it is difficult to exclude thyroid dysfunction on mere clinical background.

Various studies have been conducted on thyroid function in CRF patients. Since the beginning, the results were inconsistent. Hyperthyroidism, hypothyroidism and euthyroidism all have been reported.

The relation between thyroid dysfunction and severity of CRF is not clear. Several previous studies debit conflicting results both positive and negative.

Prevalence of hypothyroidism in end stage renal disease (ESRD) have been estimated between 0 and 9%. There is also increased prevalence of goiter in patients with ESRD.

In view of variability of thyroid function test in patients with CRF in previous studies, a prospective clinical and biochemical study on thyroid function in CRF patient in Department of Nephrology, Government Stanley Medical College Hospital, has been undertaken.

AIMS OF THE STUDY

1. To study the prevalence of thyroid dysfunction in patients with chronic renal failure.

2. To study the correlation between thyroid dysfunction and severity of renal diseases.

3. To differentiate primary thyroid diseases from thyroid dysfunction due to chronic renal failure.

REVIEW OF LITERATURE

1. PHYSIOLOGY OF THYROID HORMONES

Thyroxine (T_4) and Triiodothyronine (T_3) are the principle hormones produced by thyroid gland.

Initially iodine is absorbed in the gut and converted to iodide and transported in the blood. It is then actively transferred into the thyroid cell by "**Iodide trapping".** The trapped iodide is "**Oxidized"** to iodine and combines with tyrosine to form Mono iodotyrosine (MIT) and Diiodotyrosine (DIT). MIT and DIT are coupled to form T_3 whereas two DIT coupled to form T_4. Oxidation, Iodination and coupling reactions are catalyzed by **"Thyroid peroxidase".** Thyroid hormone thus produced are bound with thyroglobulin until secreted.(Pic.1)

Once secreted in the blood, it is transported in two forms. One is bound form, in which T_3 and T_4 are bound to plasma proteins namely thyroid binding globulin, prealbumin and albumin. T_4 is predominantly bound to thyroid binding globulin whereas T_3 is predominantly bound to albumin. The other form is free T_3 and T_4. These free forms are in equilibrium with bound form.

In the periphery one third of T_4 is converted to T_3 by **5' Deiodenase** and 45% to rT_3 by **5 deiodenase.** They are further metabolized to Diiodothyronines. Only about 13% of T_3 is produced from thyroid gland and remaining 87% is formed from T_4.

Control of thyroid hormones

The thyroid stimulating hormone (TSH) controls the secretion of T_3 and T_4. It is secreted in pulsatile manner with peak secretion at night. It's secretion is stimulated by thyrotropin releasing hormone (TRH). Both TRH and TSH release are under negative feedback of free T_3 and T_4. (Pic.2)

Hypothyroidism

Hypothyroidism is a clinical syndrome caused by decreased level of thyroid hormones. It can be **primary** in which there is intrinsic disorder of thyroid gland or it may be **secondary** in which there is pituitary or hypothalamic defect.

Florid hypothyroidism can be diagnosed clinically. The **symptoms** of hypothyroidism in descending order of frequency are:

- Tiredness, weakness
- Dry Skin
- Feeling Cold
- Hair Loss
- Difficulty in concentrating and poor memory
- Constipation
- Weight gain with poor appetite
- Dyspnea
- Hoarse voice
- Menorrhagia (Later amenorrhea)
- Paraesthesia
- Impaired hearing

The *signs* of hypothyroidism in descending order of frequency are as follows:

- Dry coarse skin
- Cool peripheral extremities
- Puffy face, hands and feet (myxedema)
- Diffuse alopecia
- Bradycardia
- Peripheral edema
- Delayed tendon reflex relaxation
- Carpal tunnel syndrome
- Serous cavity effusions

In biochemical studies, TSH is the single most important parameter for screening hypothyroidism. A normal TSH level rules out primary hypothyroidism but not secondary. To diagnose primary hypothyroidism TSH level should be above 20 μIU/ml or at least above 10 μIU/ml if clinical features strongly suggest.

In the presence of elevated TSH, low T_4 especially free T_4 is necessary to confirm hypothyroidism. Circulating free T_3 is usually reduced. But it may be normal in 25% of hypothyroid patients. So, T_3 measurements are not reliable indicators of hypothyroidism.

Hyperthyroidism

Hyperthyroidism is a clinical syndrome which results from exposure of the body tissues to excess circulating levels of free thyroid hormones.

The **symptoms** of hyperthyroidism in descending order of frequency are as follows.

- Hyper activity, irritability, dysphonia
- Heat intolerance and sweating
- Palpitations
- Fatigue and weakness
- Weight Loss with increased appetite
- Diarrhoea
- Polyuria
- Oligomenorrhea, loss of libido

The **signs** of hyperthyroidism in descending order of frequency are as follows:-

- ❖ Tachycardia; atrial fibrillation in elderly
- ❖ Tremor
- ❖ Goiter
- ❖ Warm, moist skin
- ❖ Muscle weakness, proximal myopathy
- ❖ Lid retraction or lag
- ❖ Gynaecomastia

Laboratory investigation shows TSH below normal level. Free and total thyroid hormone levels are increased.

In 2 to 5% of patients, only T_3 is increased, a condition called **"T_3 thyrotoxicosis".** Occasionally, total and free T_4 will be increased with normal T_3 level. This condition is called **"T_4 thyrotoxicosis".**

NON THYROIDAL ILLNESS[6,9,23,40,48,53]

Alteration in serum thyroid hormone occurs in wide variety of illness which predominantly affect the T_3 level in whom no intrinsic diseases of thyroid gland is detected. It was variously termed as **"Low T_3 syndrome", "Sick euthyroid syndrome", "Non thyroid illness syndrome"** and **"Thyroid hormone adaptation syndrome".**

This syndrome occurs in wide variety of illness as follows.

i. Acute critical illness and febrile illness such as infection, myocardial infarction, etc.,

ii. Injuries such as burns, trauma, etc.,

iii. Surgery

iv. Fasting

v. Diabetes Mellitus

vi. Liver disease

vii. Renal disease

viii. Ketogenic diet

ix. Drugs such as Glucocorticoids, dopamine, phenytoin and Beta Blocker

x. Malignancy

xi. Psychiatric illness

In non thyroid illness state, initially there is decrease in serum T_3 level, both total and Free T_3(FT_3) This is associated with increase in reverse T_3(rT_3).

As illness progresses, there is decrease in serum T_4 also, a state called **"low T_3, T_4 State"**. Although total T_4 level decreases, the free T_4(FT_4) remains normal or slightly reduced. In spite of this reduced T_3 and T_4 level, serum TSH level remains normal or reduced by which it is differentiated from primary hypothyroidism. But many studies have shown slight elevation of TSH level in non thyroidal illness in the absence of hypothyroidism[7,24,29].

CHRONIC RENAL FAILURE

Pathophysiology

The unique property of kidney is that in the presence of CRF, compensatory and adaptive mechanism maintain acceptable health until

the GFR is above 10 to 15 ml/min and life sustaining renal excretory and homeostatic function continues until the GFR is less than 5ml/min.

Intact nephron hypothesis

The explanation proposed for these adaptive mechanism is that in CRF there is progressive loss of nephrons, so most of the nephrons are non functioning .The remaining few functioning nephrons tend to hypertrophy and take an increased work load so that overall loss of function is minimized. This indicates that GFR of the individual functioning nephrons has increases above normal, a state known as **hyperfiltration.** This increase in single nephron GFR in functioning nephorns produce an increased volume of filtrate and their tubules respond appropriately by excreting fluids and solutes in amounts which maintain external balance. This is due to close integration of glomerular and tubular functions called "glomerulotubular balance" preserved until terminal stages of CRF. These above stated popular explanation for continuing function in remaining nephrons, is the "intact – nephron hypothesis".

Trade Off Hypothesis

It is described that adaptation arising in CRF may control one abnormality, but only in such a way as to produce other changes characteristic of uraemic syndrome. The mechanism involved is unknown. This trade off hypothesis is described in hormones like parathormone, vasopressin and ANP, solutes like sodium, potassium, phosphate and others.

Uraemic Syndrome

Uraemic syndrome is a consequence of combination of the effects of the retention of waste products in all organ system and the failure of both endocrine and hemostatic function of kidney.

The potential toxic substances that accumulate include purine metabolites amines indoles, phenols, myoinositl and acid polyols.

"Middle molecules" are nitrogenous substances of molecular weight between 50 and 5000 da. They are also suspected of contributing to uraemia.

Electrolyte and metabolic changes

Hyperkalemia usually develops when GFR falls to less than 20-25 mL/min because of the decreased ability of the kidneys to excrete potassium. It can be observed sooner in patients who ingest a potassium-rich diet or if serum aldosterone levels are low, such as in type IV renal tubular acidosis Hyperkalemia in CKD can be aggravated by an extracellular shift of potassium, such as that occurs in the setting of acidemia or from lack of insulin.

Metabolic acidosis often is mixed, non–anion gap and anion gap, the latter observed generally with CKD stage 5 but with the anion gap generally not higher than 20 mEq/L. In CKD, the kidneys are unable to produce enough ammonia in the proximal tubules to excrete the endogenous acid into the urine in the form of ammonium. In CKD stage 5, accumulation of phosphates, sulphates, and other organic anions are the cause of the small anion gap.

Extracellular volume expansion and total-body volume overload results from failure of sodium and free water excretion. This generally becomes clinically manifest when GFR falls to less than 10-15 mL/min, when compensatory mechanisms have become exhausted. Patients present with peripheral and, not uncommonly, pulmonary edema and hypertension. At a higher GFR, excess sodium and water intake could

result in a similar picture if the ingested amounts of sodium and water exceed the available potential for compensatory excretion

Hematological changes

Normochromic normocytic anemia principally develops from decreased renal synthesis of erythropoietin, the hormone responsible for bone marrow stimulation for red blood cell (RBC) production. It becomes more severe as GFR progressively decreases with the availability of less viable renal mass. No reticulocyte response occurs. RBC survival is decreased, and tendency of bleeding is increased from the uremia-induced platelet dysfunction

Bone changes

Secondary hyperparathyroidism develops because of hypocalcemia, decreased renal synthesis of 1,25-dihydroxycholecalciferol (1,25-dihydroxyvitamin D, or calcitriol), and hyperphosphatemia.

If serum levels of PTH remain elevated, a high–bone turnover lesion, known as osteitis fibrosa, develops. This is one of several bone lesions, which as a group are commonly known as renal osteodystrophy. These lesions develop in patients with severe CKD and are common in those with ESRD. Osteomalacia and adynamic bone disease are the 2 other lesions observed. The former, observed primarily from aluminum

accumulation, is markedly less common than the latter, whose etiology is unclear. Adynamic bone disease represents the predominant bone lesion in patients on chronic peritoneal dialysis and is increasing in frequency. Dialysis-related amyloidosis from beta2-microglobulin accumulation in patients who have required chronic dialysis for at least 8-10 years is another form of bone disease that manifests with cysts at the ends of long bones.

Other changes

* Pericarditis - Can complicate with cardiac tamponade, possibly resulting in death
* Encephalopathy - Can progress to coma and death
* Peripheral neuropathy
* Restless leg syndrome
* GI symptoms - Anorexia, nausea, vomiting, diarrhea
* Skin manifestations - Dry skin, pruritus, ecchymosis
* Fatigue, increased somnolence, failure to thrive
* Malnutrition

* Erectile dysfunction, decreased libido, amenorrhea

* Platelet dysfunction with tendency to bleeding

Chronic renal failure as non thyroidal illness

Chronic renal failure is one among the condition causing low T_3 syndrome.

TABLE - B

CHANGES IN SERUM THYROID HORMONES AND TSH CONCENTRATION IN PATIENTS WITH NON THYROIDAL ILLNESS

Conditions	Serum T_3	Serum rT_3	Serum T_4	Serum Free T_4	Serum TSH
Fasting	↓	↑	=	=	↓
Mild illness	↓	↑	=	=, ↑	=
Critical illness	↓	↑	↓	=, ↓	↓
Surgical trauma, burns	↓	↑	↓	↓	=, ↓
Chronic renal failure	↓	=	=, ↓	=, ↓	=, ↓
Hepatitis	=, ↑	=, ↑	=, ↑	=, ↓	=
HIV infection	=	↓	=	=, ↓	=, ↑
Depression	=, ↓	=, ↑	=, ↑	=, ↑	=, ↓

= No change, ↓ Decreased, ↑ Increased

Chronic renal failure has been divided into five stages based on the endogenous Creatinine clearance. A typical patient with chronic progressive renal diseases may be considered to pass through all 5 stages.

Stage - I : (Decreased renal reserve)

Endogenous Creatinine clearance is less than 120 ml/min. but more than 50 ml/min.

Stage - II : (Mild renal insufficiency)

Creatinine clearance is 30 – 50 ml/min. Serum Creatinine range from 2-4 mg/dl. Symptoms of mild azotemia, inability to concentrate urine, leading to polyuria and hypovolemia may be the presenting features.

Stage - III : (Moderate renal failure)

Creatinine clearance is less than 30 ml/min but more than 10 ml/min. This stage may manifest with anaemia, hypertension hyperphosphatemia, pruritis, poor intellectual performance and acidosis.

Stage - IV : (Severe renal failaure)

Creatinine clearance is less than 10 ml/min and more than 5 ml/min. Clinical manifestations similar to Stage III.

Stage - V : (End stage renal disease)

End stage renal disease is reached at glomerular filtration rate (GFR) of 5 ml/min clinical manifestations are pulmonary odema, pericarditis, hyperkalemia, fits and death. Usually serum creatinine is over 8 – 10 mg/dl.

As with other low T_3 syndromes, CRF produces decrease in T_3 when GFR falls below 50%. There is marked decrease of T_3 than T_4 as the GFR decreases. In ESRD, on average, diminished T_4 is found in 29% of the patients and diminished T_3 in 55% of the patients.

CRF as low T_3 syndrome differs from other conditions causing similar illness, by two unique features[40].

* rT_3 is usually low or normal in CRF due to redistribution into the extra vascular compartment.
* Increased incidence of goiter is present in CRF, probably due to decreased clearance of iodine by the kidney.

PATHOPHYSIOLOGY OF LOW T_3 SYNDROME

As stated above in CRF there is initial decrease in total T_3, later T_4 in spite of normal or low TSH. Various mechanism has been proposed for the change in Thyroid profile.

According to the postulates, CRF affect thyroid economy at all levels as follows.

A. Changes in Hypothalamic – pituitary – thyroid axis

i. Sensitivity of TSH secretion to low thyroid hormone is decreased.

ii. Limited TSH reserve[40]

iii. Due to changes in thyrotrophs or to decreased TRH secretion, as manifested by decrease in nocturnal pulses of TSH secretion[2,17,53].

iv. Tissue concentration of the hormone may be appropriate for the patient, so the patient is in euthyroid state[40].

v. Serum FT_3 and FT_4 appears normal by sensitive methods[3,5].

B. Changes in hormone Transport

i. Presence of protein and non protein inhibitors preventing the binding of thyroxine with thyroxine binding protein. Non protein inhibitor is non esterified unsasturated fatty acid[22,53].

ii. Acquired intrinsic structural alternation in the T_4 binding site[23].

iii. Decrease in concentration of thyroxine binding globulin[40,53].

C. Changes in metabolism

i. Decrease in the activity of lodothyronine 5 – Deiodinase leading to low T_3[40,53]

ii. Increase in Non-deiodinative pathways of iodothyronine degradation leading to increased serum T_3 sulphate, diiodotyrosine, triiodo thryoacetic acid and tetraiodothyroacetic acid[40,53].

As previously stated, there is no increase in rT_3 in CRF due to redistribution of rT_3 into extra vascular compartment[40,53].

D. Changes in plasma membrane Transport

T_3 and T_4 may enter cells not only by diffusion but also by active energy dependent transport across plasma membrane.

Accumulation of the following substances prevents uptake and subsequent deiodination.

a. 3 – carboxy 4 – methyl 5 – propyl 2 – Furane (CMPF)

b. Indoxyl sulphate

In uraemia the action of thyroid hormones at nuclear level are not compromised. Recent study showed increased receptor expression to preserve tissue Euthryroidism[52].

DIAGNOSIS OF PRIMARY THYROID DISEASES IN CRF

Recent studies have shown the prevalence of hypothyroidism is increased in chronic renal failure. And also several clinical features of both hypothyroidism and chronic renal failure are similar, so differentiating both the conditions on clinical background is less likely. Hence, all the CRF patients with symptomatology of hypothyroidism should be screened for hypothyroidism.

Hypothyroidism should be diagnosed only if the following prevails.

a. Basal TSH level should be elevated more than 20 μIU/ml.

b. Both total and free T_4 are distinctly low in the presence of normal TBG[35].

c. Presence of anti thyroid antibodies can provide clue for hypothyroidism[35].

d. rT_3 is not useful because it is decreased in CRF.

Primary hyperthyroidism is very rare in CRF. This condition is diagnosed by

a. Low serum TSH

b. High serum total and free T_4 concentration.

High serum T_4 with low T_3 in the presence of CRF should make the possibility of T_4 thyrotoxicosis. This is because serum T_3 level will be suppressed in low T_3 syndrome with serum T_4 unaffected[53].

MANAGEMENT

Several studies have been conducted in patients with the T_3 syndrome in order to correct the thyroid profile by treating with L-Thyroxine[18] and Triiodothyronine[5].

Gregory Brent et al[18] conducted study in non thyroidal illness patients by treating all the patients with serum total T_4 less than 5 μg/dl with 1.5 μg/Kg of L-thyroxine for 2 weeks. Thytroxine level increased significantly in treated patients. Serum T_3 levels were also raised. But mortality was increased in treatment group on day 5 – 17.

Carter et al[5]studied effects of Triiodothyronine administration in patients with chronic renal failure. Study showed serum T_3 level did not change over a period of 12 weeks. But the mean serum T_4 and TSH levels were affected significantly. There was no subjective improvement in these patients.

Based on this observation, it has been suggested that low serum T_3 level in patients with severe renal failure is metabolically protective and it is interpreted as physiological adaptation to reduce basal metabolic rate (BMR) and to conserve energy in an adverse environment. Hence, this

condition has been renamed as **"Thyroid hormone adaptation syndrome"[53].**

Administration of T_4 or T_3 causes suppression of TSH and increases the catabolism. So, administration of thyroid hormone is not beneficial. Study also showed increased morality with the treatment. Therefore, thyroid hormone should not be given in CRF unless true hypothyroidism can be documented.

PROGNOSIS

Magnitude of the Thyroid dysfunction that occurs in patients with chronic renal failure, in general, reflects the severity of the illness. The prognosis is poor in patients with lower serum T_3 and T_4 or TSH concentration. Studies have shown that after renal transplant the low T_3, T_4 and TSH return to normal level.

MATERIALS AND METHODS

Patients admitted to the Nephrology Ward of Government Stanley Medical College Hospital with chronic renal failure who are on conservative management.

Study design

Single Centre, Non randomized prospective study

Study period

Study was conducted between September 2006 and August 2007 for a period of 12 months.

Sample size

In the study period of 12 months among patients admitted in Nephrology ward after applying inclusion and exclusion criteria, 50 patients were included in this study.

Patients who fulfill the criteria for CRF and who are on conservative management. Thyroid profile is done in all patients who fulfilling the criteria.

Informed consent was obtained from all patients.

Criteria for Chronic Renal Failure

1. Symptoms of uraemia for 3 months or more
2. Elevated blood urea, serum creatinine and decreased creatinine clearance.
3. Ultra sound evidence of chronic renal failure
    a. Bilateral contracted kidneys – size less than 8 cm in male and size less than 7 cm in female
    b. Poor corticomedullary differentiation
    c. Type 2 or 3 renal parenchymal changes
4. Supportive laboratory evidence of CRF like anemia, low specific gravity, changes in serum electrolytes, etc.,
5. Radiological evidence of renal osteodystrophy

Exclusion criteria

1. Patients underwent pereitoneal dialysis or hemodialysis
2. Nephrogenic range of proteinuria

3. Low serum protein especially albumin

4. Other conditions like

    a. Acute illness

    b. Recent surgery, trauma or burns

    c. Diabetes mellitus

    d. Liver diseases

    e. Drugs altering thyroid profile like amiodarone, steroids, dopamine, phenytoin, beta-blocker, estrogen pills, iodine-containing drugs.

Details clinical history and clinical examination is undertaken with preference to thyroid and renal diseases. The following investigations are performed.

* Urine for specific gravity and broad cast

* Peripheral smear for anemia and burr cells

* Renal parameters like blood urea, serum Creatinine and creatinine clearance (using Cockcroft – Gault formula)

* Serum calcium and phosphorous

* Serum cholesterol for hypothyroidism
* 24 hours urine protein and serum protein to rule out nephrotic syndrome and hypoproteinemia respectively
* ECG and chest X ray to look for features for hypothyroidism and renal failure like pleural effusion, pericardial effusion
* X ray wrist, forearm and spine for evidence of renal osteodystrophy
* USG abdomen for evidence of chronic renal failure
* FNAC in patients presenting with thyroid swelling

After selecting the patients, fulfilling the above criteria, about 5 ml of blood sample is collected in nonheparinised serum bottle and sent for thyroid profile.

Components of thyroid profile in this study

* Serum triiodothyronine
* Serum thyroxine
* Serum thyroid stimulating hormone

Quantitative determination of T3, T4, TSH is done by Enzyme Linked Immunosorbent Assay.

The normal values:-

Total T3	-	0.6 to 2.1 ng/ml
Total T4	-	5 to 13 micro g/dl
TSH	-	0.4 to 7 micro IU/ml

RESULTS AND OBSERVATIONS

50 patients with CRF who were on conservative management were studied. Among 50 patients, 10 patients were female and 40 patients were male. The age varied from 12 – 70 years. Among 50 patients, 10 patients were 30 years and below, 33 patients were in the age group of 30 – 60 years and 7 patients above 60 years.

Observation regarding CRF in this study

The duration of CRF in this study varied from 3 months to 5 years. The Creatinine clearance varied from 6 ml/min to 34 ml/min. 20 patients had GFR10 ml/min accounting for 40%, 20 patients GFR 11 – 20 ml/min accounting for another 40%, remaining 10 patients accounting for 20% had GFR more than 20 ml/min.

Blood urea varied from 64 to 170 mg/dl and Creatinine varied from 3 mg to 17.2 mg/dl.

24 hours urinary protein excretion was less than 1 gm/day in all the patients in this study group.

Serum calcium and phosphorous were normal in all the patients. 80% of the patients had anaemia with peripheral smear revealing normocytic normochromic anaemia in 72% and hypochromic anaemia in 8% of the patients.

TABLE - 1

SERUM CONCENTRATION OF THYROID HORMONE

Thyroid hormones	Normal range	Study range	Mean	Std. Dev.	Mean excluding hypothyrodism	Std. Dev
Serum T_3 ng/ml	0.6 – 2.1	0.2 to 2	0.673	0.414	0.7122	0.4368
Serum T_4 µg/dl	5 – 13	0.5 to 9.5	5.622	2.27	5.99	2.08
Serum TSH µIU/ml	0.4 – 7	0.6 to 27	6.53	6.98	4.75	4.151

TABLE - 2

DISTRIBUTION OF LOW T_3 AND T_4 AMONG VARIOUS LEVELS OF TSH

TSH level µ IU/ml	No. of Patients with Low T_3	No. of Patients with Low T_4
≤ 7	16 (57.14%)	8 (53.33%)
7.1 – 20	7 (25%)	2 (13.33%)
> 20	5 (17.85%)	5 (33.33%)

TABLE - 3

ANALYSIS OF THYROID DYSFUNCTION IN THIS STUDY

Thyroid dysfunction	No. of Patients	Percentage
Low T_3 syndrome	23	46%
Low T_4 syndrome	10	20%
Hypothyroidism	5	10%

Burr cells were present in 40% of the cases. One patient had pleural effusion in this study. Two patients in this study showed evidence of osteodystrophy.

Ultra sound abdomen showed evidence of CRF in all patients contracted kidney was present in 90% of the patients. Remaining patients had poor corticomedullary differentiation.

Among the 50 patients, low serum T_3 level was found in 28 patients (56%), 5 patients among the low serum T_3 level also had high TSH value more than 20 μIU/ml with low T_4 level and also symptoms suggestive of hypothyroidism.

These patients as per the criteria were grouped under "primary hypothyroidism". Remaining 6 patients had slightly elevated TSH ranging between 9 and 14 μIU/ml. In these 6 patients, only 3 patients had low T_3 level, among which only one patient had few clinical features of hypothyroidism. So, these 6 patients didn't satisfy the criteria for hypothyroidism fully. So all 23 patients were grouped under "Low T_3 syndrome" of "sick Euthyroid syndrome".

Features of hypothyroidism in CRF

Symptoms of hypothyroidism like tiredness, somnolence, weight gain, cold intolerance, constipation, hoarseness of voice etc., were studied in CRF in the study population. 35 patients (70%) had the symptoms (Table - 7). Among the 35 patients, 5 of the hypothyroid patients had the symptoms (83.33%), 17 (73.91%) of low T_3 syndrome patients had the hypothyroid symptoms in CRF without Thyroid dysfunction, 13 patients (59.09%) had the symptoms.

TABLE - 4

ANALYSIS OF SERUM T_3 T_4 AND TSH EXCLUDING HYPOTHYROIDISM

Thyroid dysfunction	No. of Patients with Normal values	%	No. of Pt with low values	%	No. of pt with high values	%
T_3	22	44%	23	46%	NIL	NIL
T_4	35	70%	10	20%	NIL	NIL
TSH	38	76%	NIL	NIL	7	14%

TABLE - 5

AGE INCIDENCE OF LOW T_3 SYNDROME IN THIS STUDY

Age in years	No. of Patients	Low T_3 syndrome	Percentage
$\leq$ 30	10	3	30%
31 – 60	33	17	51.50%
> 60	7	3	42.85%

TABLE - 6

SEX INCIDENCE OF LOW T_3 SYNDROME IN THIS STUDY

Sex	No. of patients	Low T_3 Syndrome	Percentage
Male	40 (80%)	20	50%
Female	10 (20%)	3	30%

Dry, flaky skin was present in 15 patients of which only 4 patients were hypothyroid.

Sinus bradycardia was present in 7 patients of which only 2 patients were hypothyroid. Delayed ankle jerk was present in 8 patients of which only 2 patients were hypothyroid.

Hypothyroidism didn't show any linear correlation with GFR. Increased number of hypothyroid patients of about 4 in number were present in GFR 11 – 20 ml/min whereas only 2 patients had hypothyroidism in GFR less than 10 ml/min.

In our study, diffuse thyroid swelling was present in one patient. Both of these patients had low T_3 syndrome with normal TSH level. FNAC of the thyroid swelling showed features of goiter. This is insignificant in the study.

Age comparison of Low T_3 syndrome in table-5 shows about 30% of CRF patients below 30 years of age have low T_3 syndrome. The percentage increases to 51.51% in the age group 31 – 60 years. This is probably due to increased CRF patients in this age group. In age above 60 years, 42.85% have low T_3 syndrome.

Sex incidence in this study (Table-6) shows 50% of males have low T_3 syndrome and only 30% of the females have low T_4 syndrome.

Observation of T_3 in this study

T_3 level in this study varied from 0.2 to 2 ng/ml. The mean value of T_3 is 0.67 ng/ml (Table-1). Excluding the patients with primary hypothyroidism, the mean value is 0.71 ng/ml. This value was in low normal limit. Excluding hypothyroidism T_3 levels were studied in relation to GFR. It was found that mean value of serum T_3 is low (0.538 ng/ml) only in patients with GFR less than 10 ml/min (Table – 10). The mean value is low normal in patients with GFR more than 10 ml/min. According to our study, number of patients with low T_3 increase with increase in severity of the renal failure (Table-8) in spite of low T_3 levels.

Observations of T4 in the study

Serum T4 level in the study varies from 0.5 to 9.5 μg/dl. Mean value of serum T_4 among 50 patients 5.62 μg/dl Excluding hypothyroid patients, the mean value is 5.99 μg/dl. This value is within low normal level of T4.

TABLE - 7

ANALYSIS OF HYPOTHYROID SYMPTOMS IN CRF

Variants	**No. of patients with symptoms**	**Percentage**
Low T_3 Syndrome (n=23)	17	73.91%
Hypothyroidism (n=5)	5	100%
CRF without thyroid dysfunction (n=22)	13	59.09%

TABLE - 8

DISTRIBUTION OF LOW T_3 AND T_4 SYNDROME IN THIS STUDY

Creatinine Clearance ml/min	Low T_3 Syndrome		Low T_4 Syndrome	
	No. of Patient	Percentage	No. of patient	Percentage
$\leq$ 10	13	65%	6	30%
11 – 20	7	35%	3	15%
> 20	5	30%	1	10%

TABLE - 9

DISTRIBUTION OF THYROID DYSFUNCTION IN THIS STUDY AMONG VARIOUS CREATININE CLEARANCE LEVELS

Creatinine Clearance ml/min	No. of Patients	Low T_3 Syndrome	Hypothyroidism
$\leq$ 10	20 (40%)	13 (65%)	3 (15%)
11 – 20	20 (40%)	7 (35%)	2 (10%)
> 20	10 (20%)	3 (30%)	NIL

TABLE - 10

CORRELATION OF THYROID HORMONES WITH SEVERITY OF RENAL FAILURE EXCLUDING HYPOTHYROIDISM

Creatinine Clearance ml/min	**Mean T_3 µg/dl**	**Std. Dev**	**Mean T_4 µg/dl**	**Std. Dev.**	**Mean TSH µIU/ml**	**Std. Dev**
≤ 10 (n=17)	0.538	0.40	5.02	2.10	5.22	4.25
11 – 20 (n=18)	0.82	0.43	6.69	2.17	3.77	3.78
> 20	0.8	0.31	6.32	2.04	5.72	5.00

Excluding 5 hypothyroidism patients who have low T4 values, 9 (21.33%) other patients had T4 level below normal and low T3 syndrome.

Number of patients with low T4 does not correlate with severity of renal disease (Table 8). The mean value of T4 excluding hypothyroidism patients was normal at all the stages of renal failure (Table 9).

None of the patients had T4 value above normal level.

Observation of TSH in the study

Values of TSH vary from 0.6 to 27 μIU/ml with mean value in 6.53 μIU/ml. Excluding hypothyroidism mean value is 4.75 μIU/ml. This shows normal serum level of TSH.

Among the 50 patients, TSH was normal in 38 patients (76%) and values between 7.1 – 20 μIU/ml in 7 patients (14%). It was elevated more than 20 μIU/ml in 5 patients (10%).

According to our study, in patients with low T_3 syndrome, the mean values of TSH in various stages of renal failure are within normal range. But the values of TSH didn't show any linear correlation with GFR.

DISCUSSION

Thyroid dysfunction in CRF was extensively studied by **Ramirez[37].**

Apart from his study, various studies conducted in this line have showed different results.

In our study, patients only on conservative management were studied. This is because thyroid profile undergoes changes due to dialysis independent of that due to chronic renal failure. Dialysis also changes the previous serum status of thyroid hormone in the patients with renal failure. Many studies have conducted by comparing CRF patients conservative Management and Hemodialysis by **Ramirez[42] and kayima et al[29].**

Many studies conducted in CRF patients showed low T_3 values. Low T_3 had been reported in **Ramirez et al[37], Hegedus et al[21], Beckett et al[37,21,2]** studies, that to in severe renal failure. **Ramirez and spectar et al[37]** study showed linear correlation between the mean serum T_3 and T_4 and severity of renal failure.

As with other studies, mean T_3 level in our study was reduced below normal in GFR less than 10 ml/min. In higher GFR, it was present in low normal and there was no linear correlation between T_3 level and GRF, which is consistent with **Avasthi et al study[1].**

Mean T_4 level in our study is within normal limits in all levels of GFR, but it is in low normal level and also it does not correlate with the severity of renal failure.

In our study, not all the patients with CRF have low T_3 and T_4. It is estimated that only 58% (29 patients) of patients have Thyroid Profile abnormality. Remaining 42% of patients have normal thyroid profile.

Among 58% of these patients exclude primary hypothyroid patients 28% have only low T_3 level with normal T_4 level. Remaining 20% have both low T_3 and T_4 level. The percentage of patients having low T_3 and T_4 gradually increase, with decrease in GFR. The patient who will develop such change in thyroid profile is not known.

Excluding hypothyroidism, mean TSH level in our study is within normal limits. The mean TSH levels are also within normal limits for the various ranges of GFR. But TSH level doesn't show any linear correlation with the severity of renal failure. This is consistent with the

study conducted by **Spector and Ramirez et al[49,37].** These studies demonstrated abnormality in hypophyseal mechanism of TSH release in uraemic patients as the as the TSH response to the TRH was blunted.

Other studies conducted by **Joseph et al and Hardy et al[24,19]** revealed low T_3 T_4 level with high TSH level suggesting maintenance of pituitary thyroid axis.

In our study, excluding those with hypothyroidism, seven patients had mild elevation of TSH with low T_3 level. Among these patients, T_4 is within normal limits in 4 of the patients. In the remaining 3 patients T_4 is below normal. There were no clinical features suggestive of hypothyroidism in these patients. Investigations like FT_4, FT_3 TRH response and anti thyroid auto antibodies can be done to diagnose hypothyroidism in these patients.

Out study is consistent with the results of **Ramirez et al[37]** study showing low T_3, low T_4 and normal or mild elevation of TSH. Yet it is unclear that to what extent these changes are responsible for the manifestations of Uraemic syndrome. From the various studies it has been suggested that this thyroid profile derangements is a part of body adaptation mechanism.

Dialysis

As stated previously, Hemodialysis and continuous ambulatory peritoneal dialysis have shown to affect the thyroid profile independently of CRF. Also drugs like heparin, furosemide used during dialysis will affect the thyroid profile.

Kayima et al[29] and **Giordano et al**[16] have conducted studies regarding effect of dialysis on CRF patients with thyroid dysfunction. These study showed no significant improvement in thyroid profile after repeated hemodialysis.

But in the patients who have undergone renal transplant surgery, most of the thyroid function parameters returned to normal with TSH below normal[55].

Hypothyroidism

Previous studies by **Quion verde et al**[36] reported high prevalence of hypothyroidism in CRF. It was estimated to be about 5% in patients with terminal renal failure.

Detail study by **Kaptein et al**[25,26] estimated the prevalence of primary hypothyroidism was about 2.5 times much frequent in chronic

renal failure and dialysis. The hypothyroidism in CRF was estimated to range between 0 and 9.5% Kaptein study also estimated the presence of anti thyroid antibody titer in 6.7% of CRF.

In our study, the hypothyroidism is present in 10% of the patients but doesn't correlate with the severity of the renal failure. The symptoms of hypothyroidism were distributed equally in both hypothyroid and CRF patients in our study. Signs of hypothyroidism were more common in CRF without hypothyroidism than with hypothyroidism.

So, diagnosis of hypothyroidism in CRF mainly rest on TSH level which should be very high (> 20 MIU/dl) with low serum T_4.

In this study no patient had clinical or biochemical features of hyperthyroidism.

Goiter

Ramirez et al[42] reported high prevalence of goiter in CRF patients especially those on chronic dialysis. Incidence were increased in end stage renal disease. The possible explanation is due to accumulation of iodides in Thyroid gland due to decreased renal clearance in CRF patients. Apart from goiter, study conducted by **Hegedus et al**[21] showed thyroid gland volume was significantly increased in patients with CRF.

In our study, only 1 patient had goiter without any clinical or biochemical feature of hypothyroidism. This patient had low T_3 level with normal TSH and T_4. The number of patients with goiter in our study is statistically insignificant.

CONCLUSIONS

1. Thyroid dysfunction occurs in 58% of the chronic renal failure patients.

2. Incidence of hypothyroidism is increased in patients with chronic renal failure.

3. Both clinical and biochemical parameters are essential to diagnose hypothyroidism in patients with CRF.

4. Excluding patients with hypothyroidism T_3 level is low in 46% of the patients, T_4 level is low in 20% of the patients.

5. Number of patients with low T_3 and T_4 syndrome progressively increase with severity of renal failure.

6 Serum level of T_3 and T_4 has no correlation with the severity of renal failure.

7. Alteration in the values of T_3 and T_4 occurs as a part of body adaptations mechanism to conserve energy.

BIBLIOGRAPHY

1. **Avasthi G et al,** (2001) Study of Thyroid function in patients of chronic renal failure. **Indian Journal of Nephrology, 11:165 – 170**

2. **Beckett G et al,** (1983). Thyroid status in patient with chronic renal failure. **Clinical Nephrology, 19: 172 – 8**

3. **Bartalena L et al,** (1990). Lack of nocturnal serum Thyrotropin surge in patients with chronic renal failure undergoing regular maintenance hemofiltration; a case of central hypothyroidism. **Clinical Nephrology, 34: 30 – 4.**

4. **Biersack HJ et al, (1976),** Thyroid hormones and thyrotropin in liver and kidney insufficiency. **J Nuclear Medicine 15: 135 – 7.**

5. **Carter JN et al,** (1977). Effects of triiodothyronine administration in patients with chronic renal failure. **AUST NZ J Med, 7:612 – 6.**

6. **Custro N et al,** (1992). Prospective study on thyroid function anomalies in seriously ill patient. **Ann Ital med Int 7:13 – 8 .**

7. **Dandona P et al,** (1976). Thyroid function in chronic renal failure. **Proc Eur Dial transplant Assoc, 12:268 – 71.**

8. **Davidson's Principle and Practice of Medicine,** 18th Edition. The thyroid gland.

9. **Degroot.** The thyroid and its diseases, 6th Edition. Non-Thyroidal illness.

10. **De Soousa FT et al.** (1988). Study of the thyroid function in patients with chronic renal insufficiency in hemodialysis. **Acta med port 1:247 – 50**

11. **Drabezyk R et al.** (1993). Function of the pituitary – thyroid in chronic renal failure. **Postepy Hig med Dosw, 47:177**

12. **Dudani RA et al.** (1981). Thyroid dysfunction in Ureaemia **J Assoc Physicians India. 29: 1037 – 40.**

13. **Fankhauser S et al.** (1967). Repercussions of renal insufficiency on the endocrine organs and especially on the thyroid function. **J urol Nephrol. 73: 767 – 80.**

14. **Forest SC et al,** (1982). Thyroid hormones in patients with chronic renal failure undergoing maintenance hemodialysis.**Am J clin pathol,77:580 – 6.**

15. **Gaskin JH,** (1976).Thyroid gland in uraemia. **Am Intern Med. 85:680 – 1**

16. **Giordano C et al,** (1984). Thyroid Status and nephron loss – a study in

17. patients with chronic renal faialure, end stage renal disease and/or on

18. hemodialysis. **Int J Artif organs 7;119 – 22.**

19. **Gomez-pan A et al.** (1979). Function of the hypothalamo-hypophysial-

20. Thyroid axis in chronic renal failure. Clin Endocrinology, 11;567 – 74

21. Gregory A. Brent et al. (1986). Thyroxine therapy in patients with severe non thyroidal illness and low serum thyroxine concentration. **J clin Endo and met 63:1 – 8.**

22. **Hardy MJ et al** (1988) Pituitary – Thyroid function in chronic renal failure assessed by a highly sensitive thyrotropin assay. **J clin Endocrinol metab, 66:233 – 6.**

23. **Hasegawa K et al,** (1975). Abnormal response of thyrotrophin and growth hormone to thyrotrophin releasing hormone in chronic renal failure. **Acta Endocrinol 79:635 – 43.**

24. **Hegedus L et al,**(1985). Thyroid gland volume and serum concentrations of thyroid hormone in chronic renal failure. **Nephron, 40:171 – 4.**

25. **Inder J. Chopra et al,** (1986). Serum Thyroid hormone binding inhibitor in Non thyroidal illness. **Metabolism, 35.**

26. **John T. Nicoloff et al.** Non thyroidal illness. Degroot's Endocrinology, 3rd Edition. Volume 1.

27. **Joseph L.J. et al,** (1993). Measurement of serum thyrotropin levels using sensitive immunoradiometri assays in patients with chronic renal failure alterations suggesting an intact pituitary thyroid axis.**Thyroidology 5:35- 9.**

28. **Kaptein E et al,** (1988). The Thyroid in end stage renal diseases, **Medicine 67:187 – 97.**

29. **Kaptein E et al,** (1986). Thyroid function nin renal failure. **Contrib Nephrol, 50:64 – 72.**

30. **Karunanidhi A et al,** (1979). Thyroid function in patients with chronic renal failure. **Indian J Med Research, 69:792 – 7.**

31. **Katz Al et al,** (1975). Thyroid hormones and the kidney. **Nephron 15:223 – 49.**

32.Kayima JK et al, (1992). Thyroid hormones profile in patients with chronic renal failure on conservative management and regular hemodialysis. **East Afr Med J, 69:333 – 6.**

33.Kolendorf K et al. (1978). The influence of chronic renal failaure on serum and urine thyroid hormone level. **Acta Endocrinol, 89:80 – 8.**

34.Labos I et al, (1979). Disturbance of thyroid gland function in chronic renal failure. **Med arh 33:183 –7.**

35.La Franchi S et al, (1991). Thyroid function in children with renal failure. **J Pediatr. 118:896 – 8.**

36.**Lim VS et al,** (1977). Thyroid dysfunction in chronic renal failure. A study of the Pituitary thyroid axis an peripheral turnover kinetics of thyroxine and triodo thyroxine. **J clin Invest 60:522 – 34.**

37.**Mehta HJ et al,** (1991). Total and free thyroid hormone levels in chronic renal failure. **J Post Grad Med. 37(79 – 83).**

38.Oxford text book of clinical Nephrology, 2nd Edition, Volume-3, The patient with failing renal function.

39.Quion-verde et al, (1984). Prevalence of thyroid disease in chronic renal failure and dialysis patients. **IXth Int Congr of Nephrol, 120.**

40.Ramirez G et al, (1976). Thyroid dysfunction in uraemia. Evidence for thyroid and hypophyseal abnormalities. **Ann Inter med 84:672 – 6.**

41.Ramirez G et al, (1973). Thyroid abnormalities in renal failure. A study of 53 patients on chronic dialysis. **Ann Internal medicine, 79, 500 – 4.**

42. **Rao MB et al,** (1986). Primary hypothyroidism in chronic renal failure. **Clin Nephrol, 25:11 – 4**

43. Reed Larsen P et al. The thyroid gland. Williams's textbook of Endocrinology. 9th Edition.

44. Rubio Perez P et al. (1980). Thyroid hormone changes in patients with non-advances renal failure. **Rev Clin Esp, 157: 163 – 6.**

45. **Ramirez et al.** (1972). Thyroid function in chronic renal failure. Effect of chronic hemodialysis. **Trans Am Society of Art Org, 18:244 – 9.**

46. Rudolf K et al, (1988). Behaviour of the basal and stimulated serum level of thyroid stimulating hormone and determination of Thyroxine, thyroxine binding capacity and free thyroxine index in females with chronic uraemia.

47. Sicinski A (1972). Thyroid Function in chronic renal failure. **Pol Arch Med. 49:607 – 16.**

48. Silverberg DS et al, (1973). Effect of chronic hemodialysis on thyroid function in chronic renal failure. **Can Med an 109:282 – 6.**

49. Vaziri ND et al, (1981). Thyroid function in chronic renal failure after successful renal transplant. **Clin Nephrol 15:131 – 4.**

50. Wassner SJ et al, (1977). Thyroid function in children with chronic renal failure. **Nephron, 19:236 – 41.**

51. Weissel M, (1978). Evaluation of thyroid function in non thyroid diseases. **Acta Med Austrica 5:100 – 2.**

52. Spector DA et al, (1976). Thyroid function and metabolic rate in chronic renal failure. **Ann Intern Med. 85:724 – 30.**

53. **Weissel M et al** (1979). Basal and TRH stimulated Thyroid and Pituitary hormones in various degree of renal insufficiency. **Acta Endocrinol 90:23 – 32.**

54. William F Ganong, Review of medical physiology, 17th Edition, The Thyroid Gland.

55. **William GR et al.** (1990). Thyroid hormones receptor expression in the "Sick enthyroid syndrome". **Lancet, 335 : 662 –3.**

56. Willmar M. Wiersingh, Non Thyroidal illness, Werner and Ingbar's The thyroid, 8th Edition.

57. **Yashpal,** (1991). Thyroid function in Uraemia. **Ind.J. of Neph. 2:1 – 2.**

58. CRF – Hormones Principle Medicine

59. **Lim VS,** (2001). Thyroid functions in patients with CRF. **Am. J of Kidney disease 38; 80 – 84.**

PROFORMA

Name: Age: Sex: IP No:

Occupation: Address:

Past H/O:

HT: Y/N

DM: Y/N

Recent surgery/Trauma: Y/N

Drugs: Y/N

Jaundice: Y/N

Other systemic illness: Y/N

Menstrual and Obstetric History:

General Exam:

1. Nourishment:
2. Pallor:
3. Hyper pigmentation:
4. Facial puffiness:
5. Pedal edema:
6. Skin texture:
7. Thyroid swelling:

Pulse:

BP:

Respiratory rate:

Temperature:

CVS:

RS :

Abdomen :

CNS :

Investigations:

1. Urine complete examination:
2. Blood:

Hb: gm/dl
TC:
DC: P %L %E %
RBC: Cells/cumm
BT: mnte
CT: mnte
Peripheral smear

3. Blood

Urea:

Creatinine:

Na:

K:

Ca:

PO4:

Serum Cholesterol

Serum protein Total

Albumin

Globulin

4. ECG

5. X-rays

    Chest X-ray

    X-ray wrist, forearm, vertebral spine

6. USG abdomen

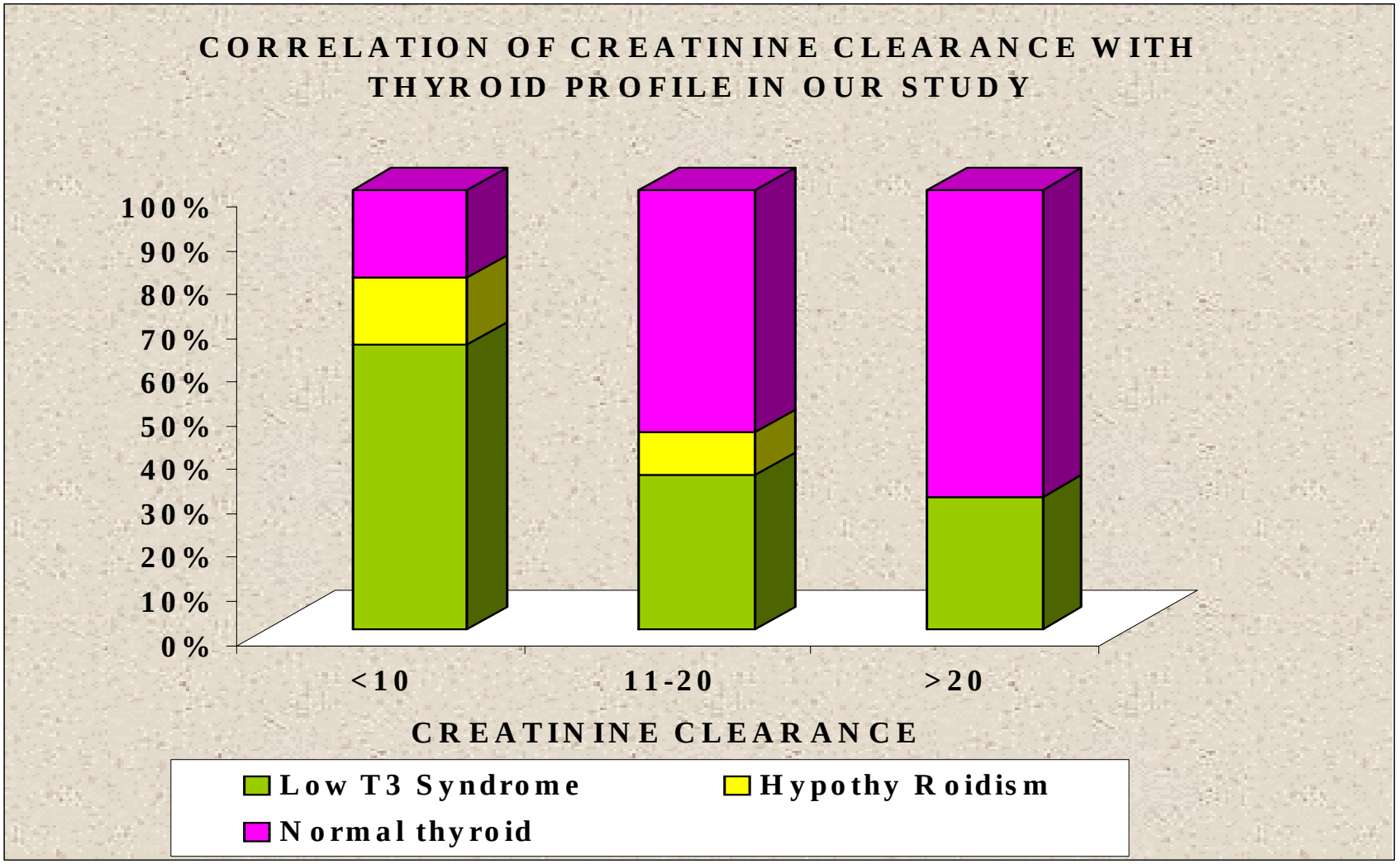
7. 24 hrs urine protein

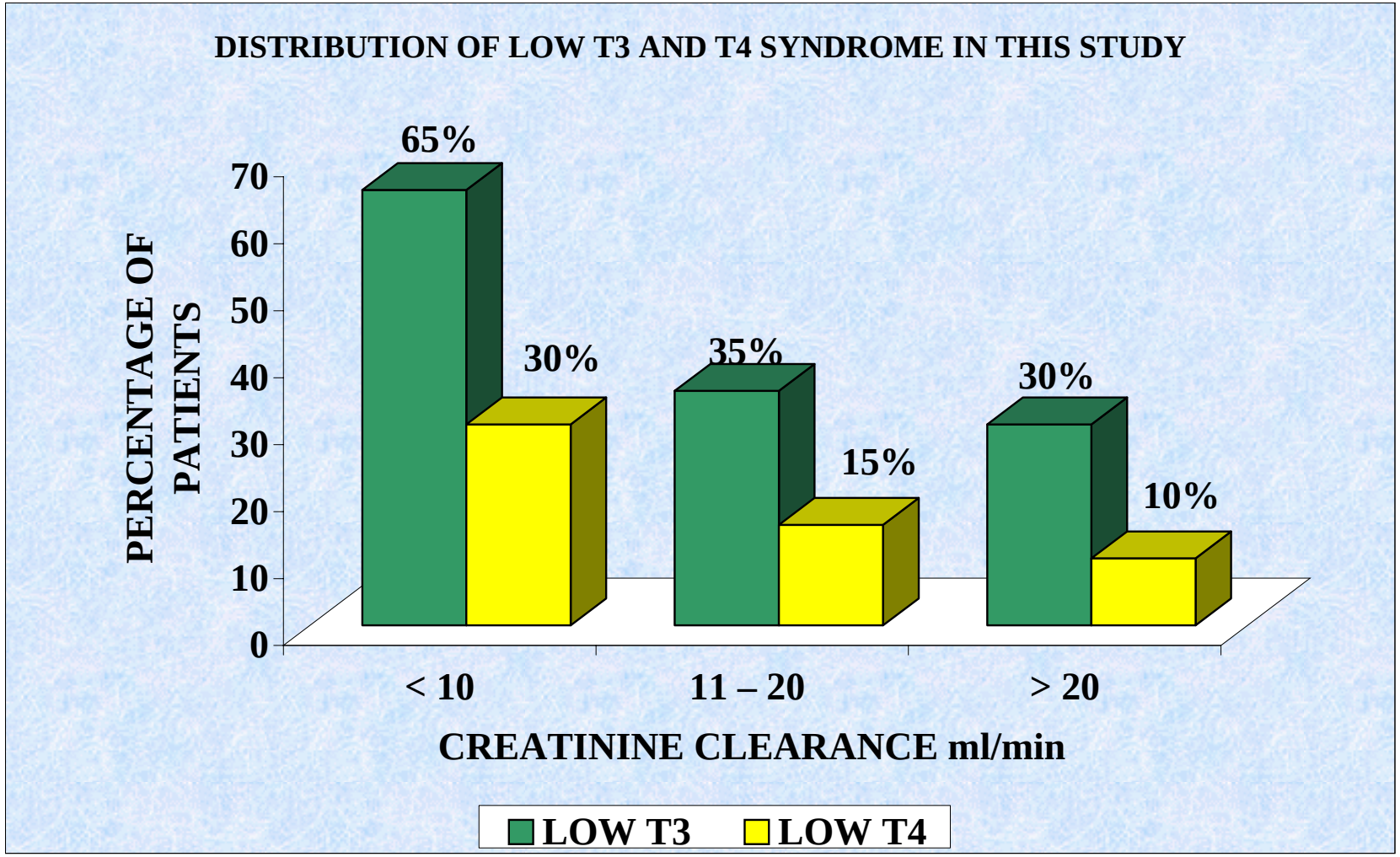
8. Thyroid profile

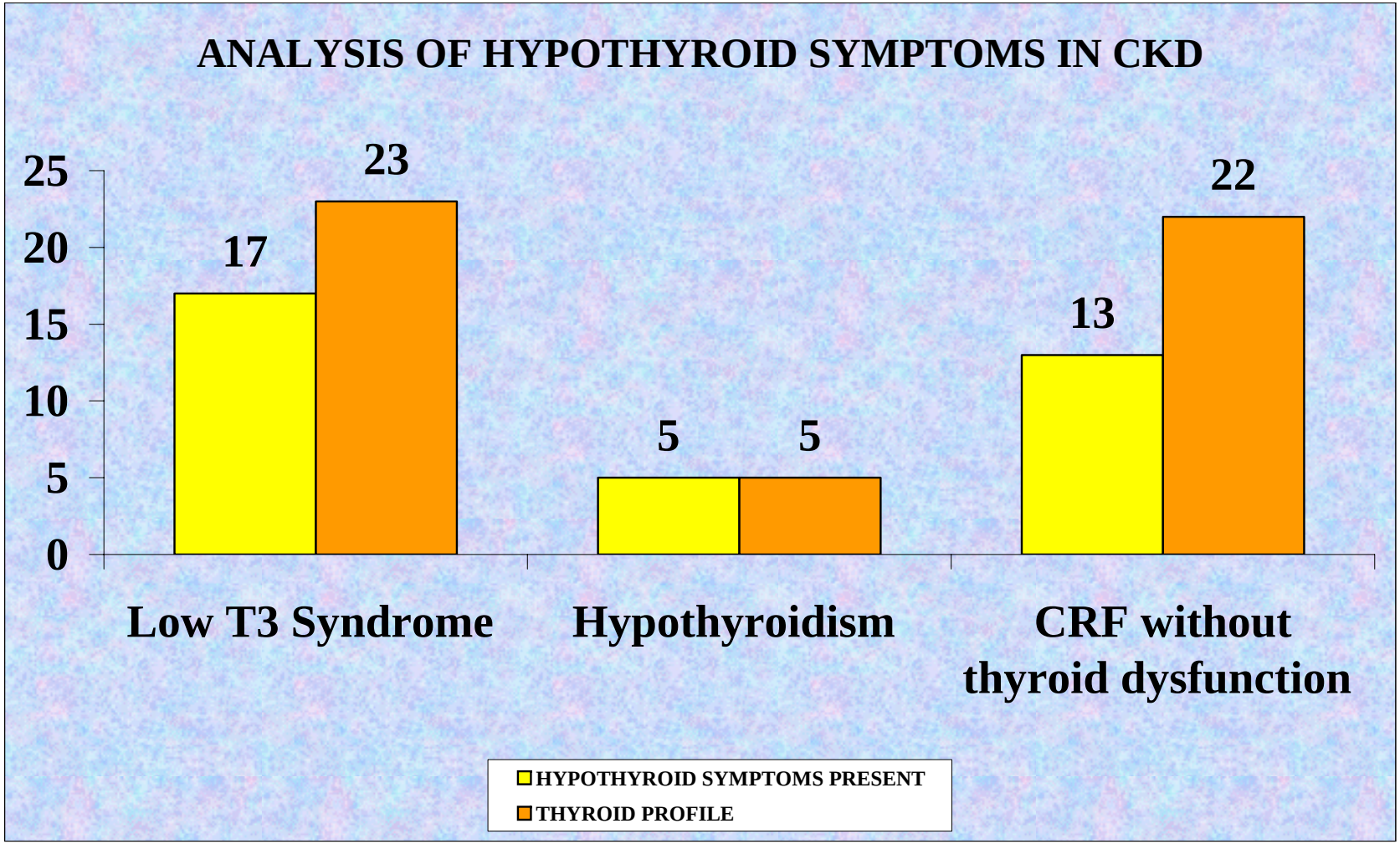
    Serum triiodothyroine

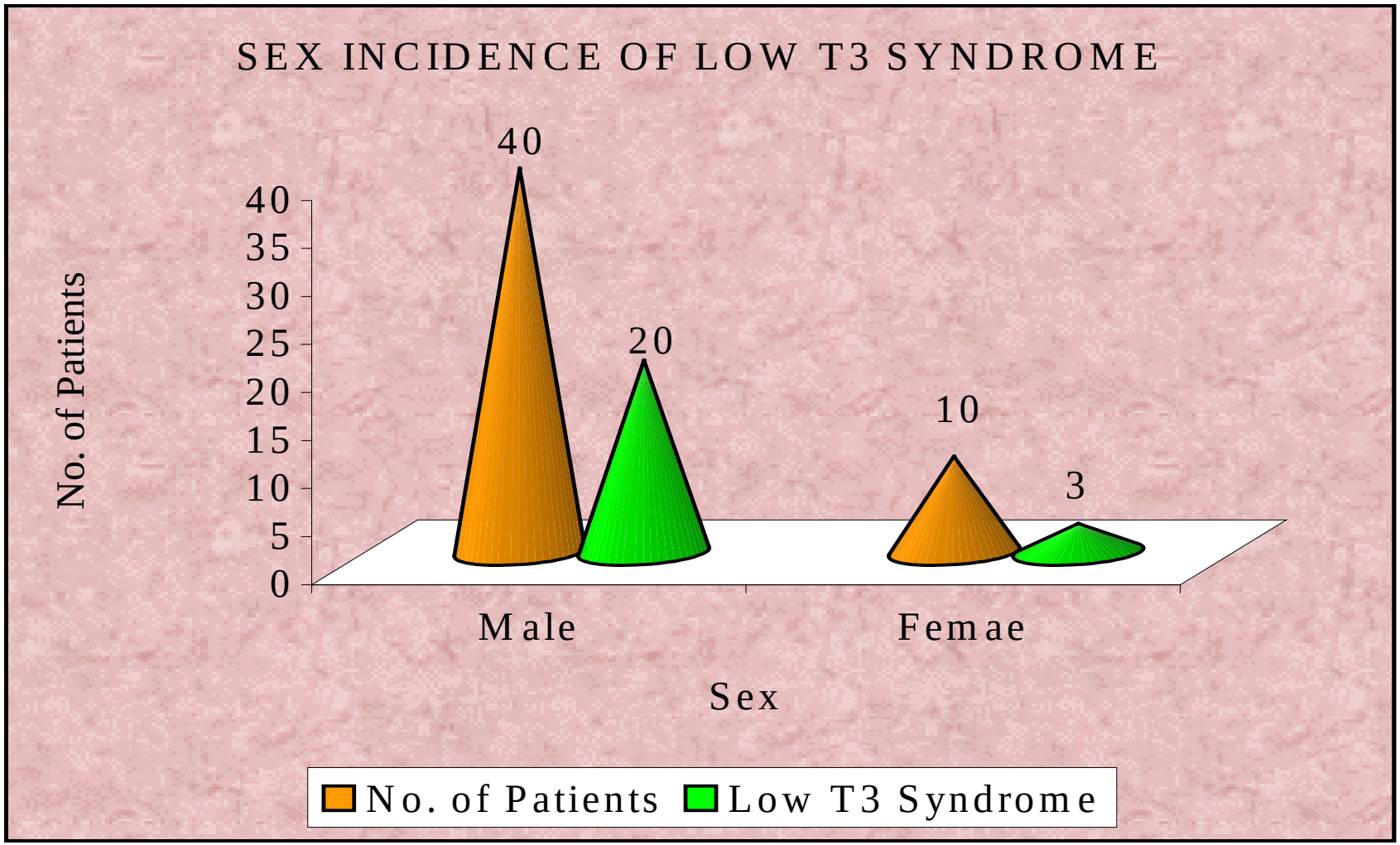
    Serum thyroxin

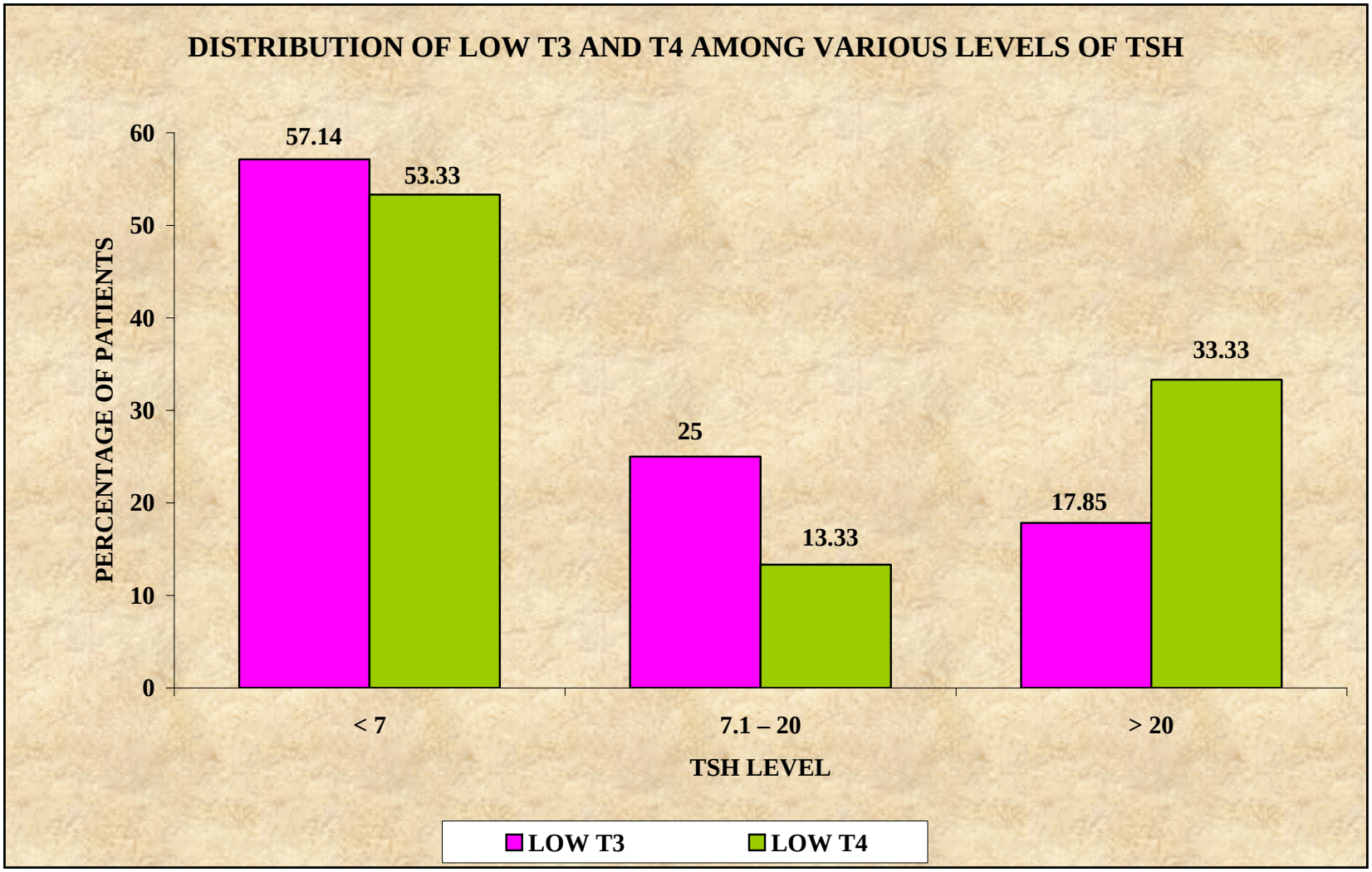
    Serum thyroid stimulating hormone

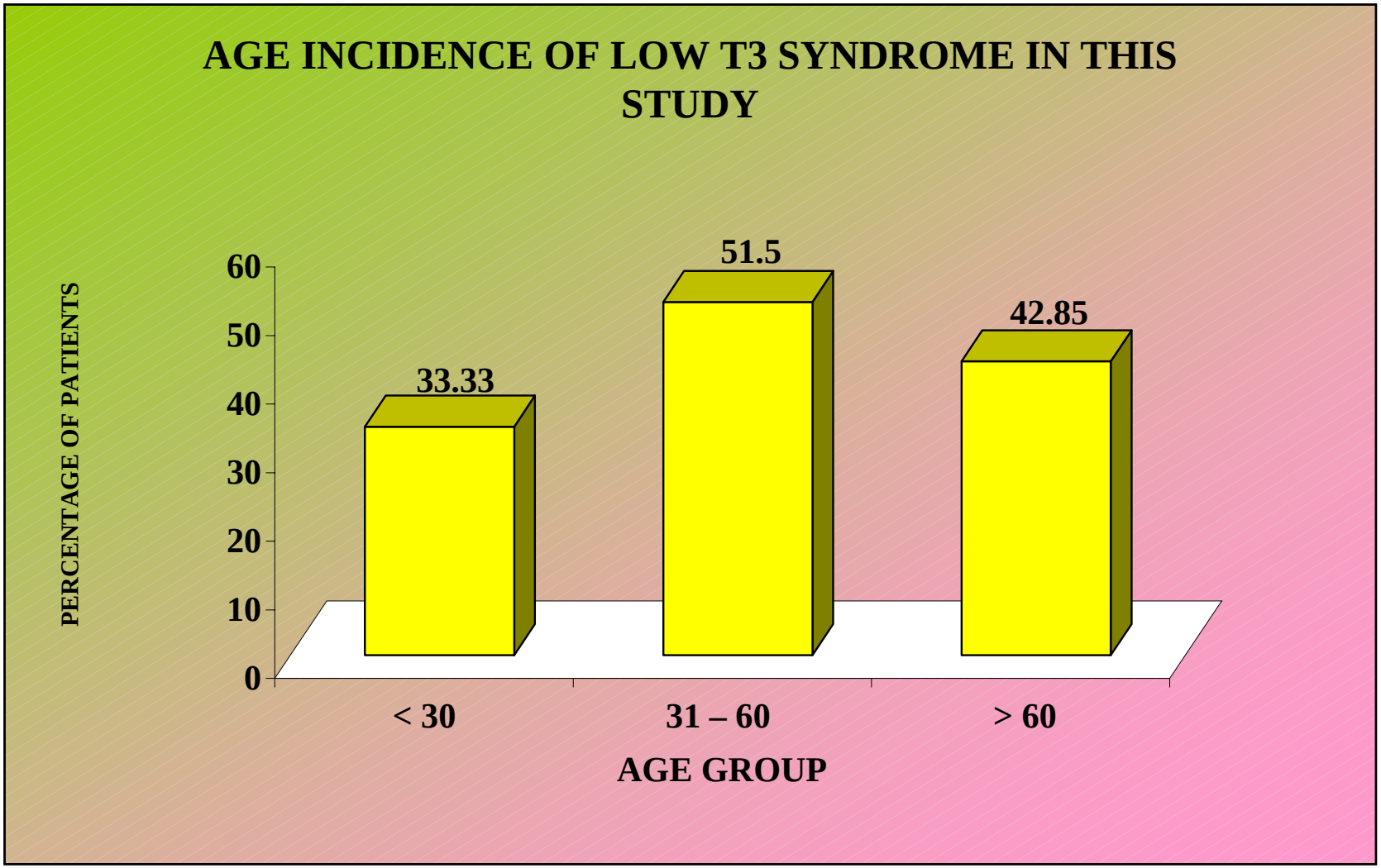

CORRELATION OF CREATININE CLEARANCE WITH THYROID PROFILE IN OUR STUDY
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
<10
11-20
>20
CREATININE CLEARANCE
Low T3 Syndrome
Hypothy Roidism
Normal thyroid

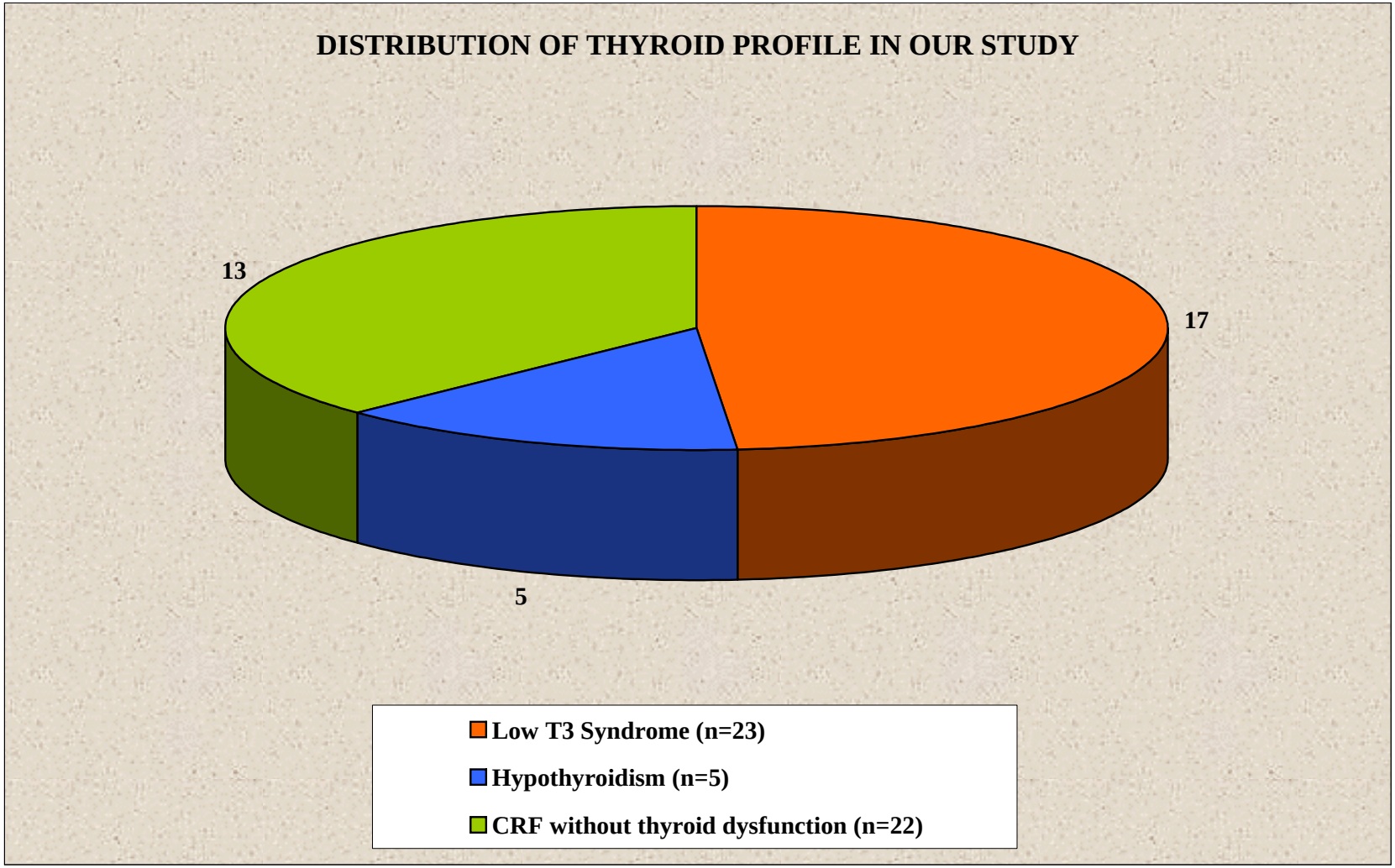

DISTRIBUTION OF LOW T3 AND T4 SYNDROME IN THIS STUDY
PERCENTAGE OF PATIENTS
70
60
50
40
30
20
10
0
65%
30%
35%
15%
30%
10%
< 10
11 – 20
> 20
CREATININE CLEARANCE ml/min
LOW T3
LOW T4

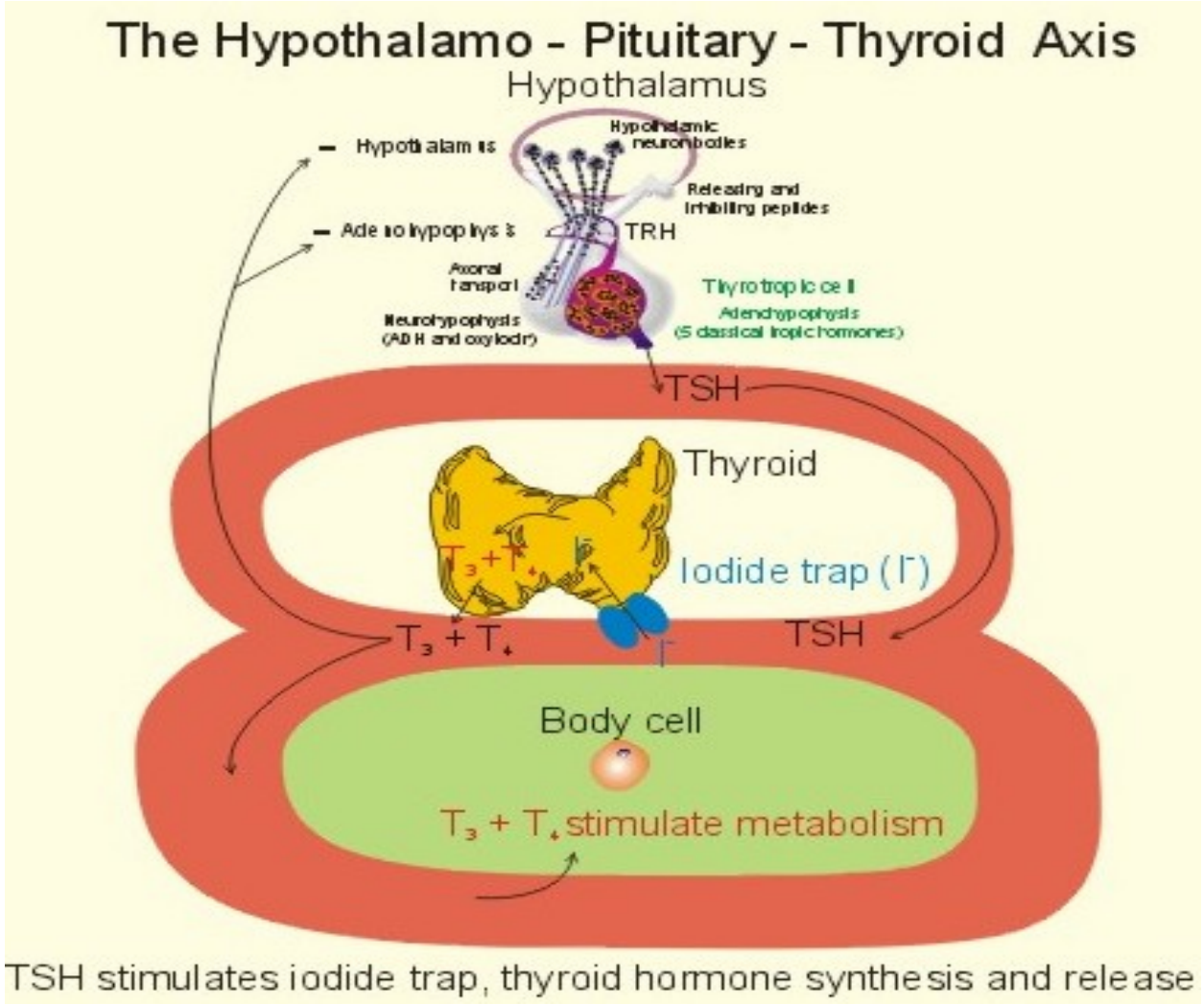

ANALYSIS OF HYPOTHYROID SYMPTOMS IN CKD
25
20
15
10
5
0
17
23
5
5
13
22
Low T3 Syndrome
Hypothyroidism
CRF without thyroid dysfunction
HYPOTHYROID SYMPTOMS PRESENT
THYROID PROFILE


SEX INCIDENCE OF LOW T3 SYNDROME
No. of Patients
40
35
30
25
20
15
10
5
0
40
20
10
3
Male
Femae
Sex
No. of Patients
Low T3 Syndrome


DISTRIBUTION OF LOW T3 AND T4 AMONG VARIOUS LEVELS OF TSH
PERCENTAGE OF PATIENTS
60
50
40
30
20
10
0
57.14
53.33
25
13.33
17.85
33.33
< 7
7.1 – 20
> 20
TSH LEVEL
LOW T3
LOW T4


AGE INCIDENCE OF LOW T3 SYNDROME IN THIS STUDY
PERCENTAGE OF PATIENTS
60
50
40
30
20
10
0
33.33
51.5
42.85
< 30
31 – 60
> 60
AGE GROUP


DISTRIBUTION OF THYROID PROFILE IN OUR STUDY
13
17
5
Low T3 Syndrome (n=23)
Hypothyroidism (n=5)
CRF without thyroid dysfunction (n=22)



TSH stimulates iodide trap, thyroid hormone synthesis and release

Thyroid Hormone Synthesis by Thyroid Follicle Epithelial Cells

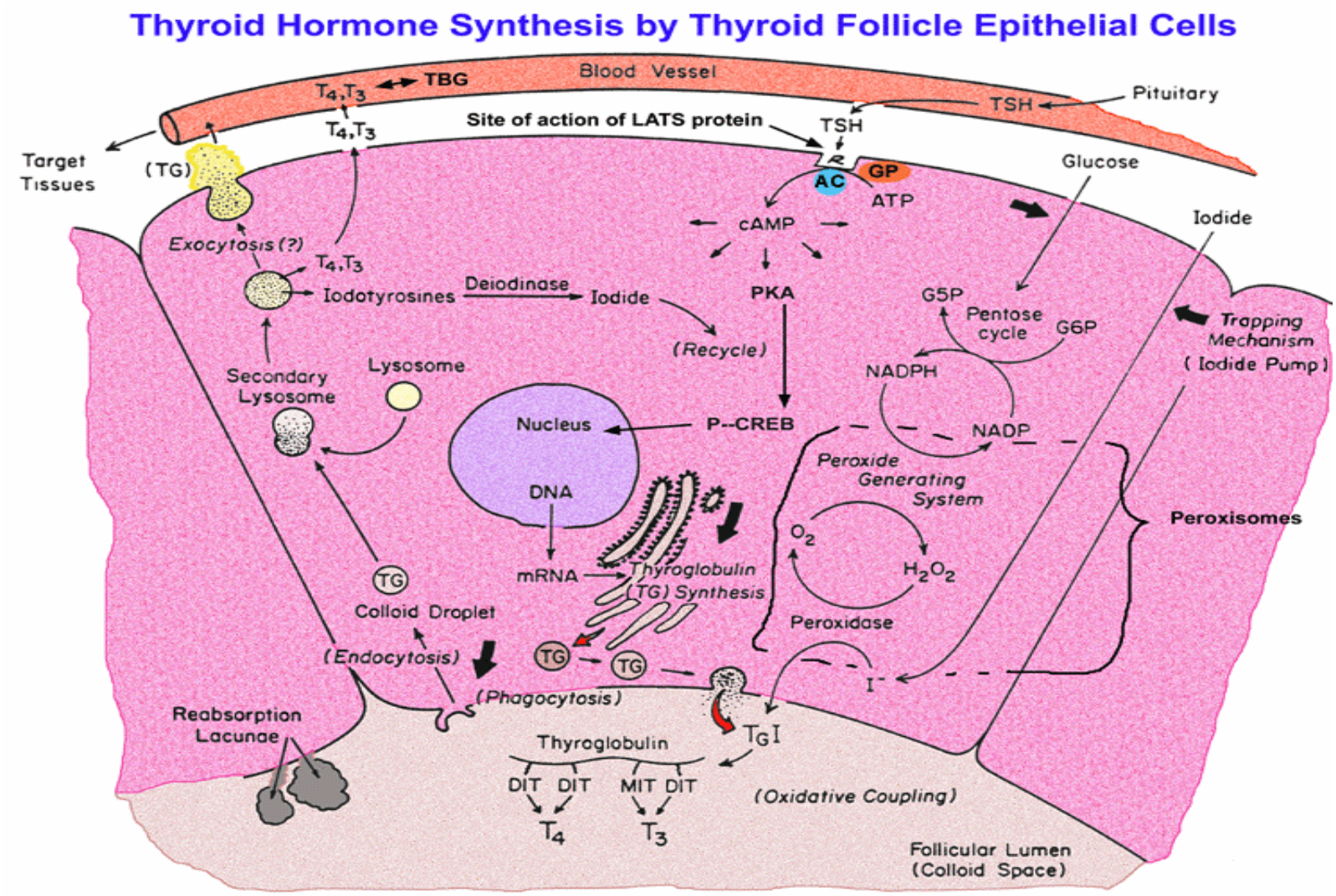
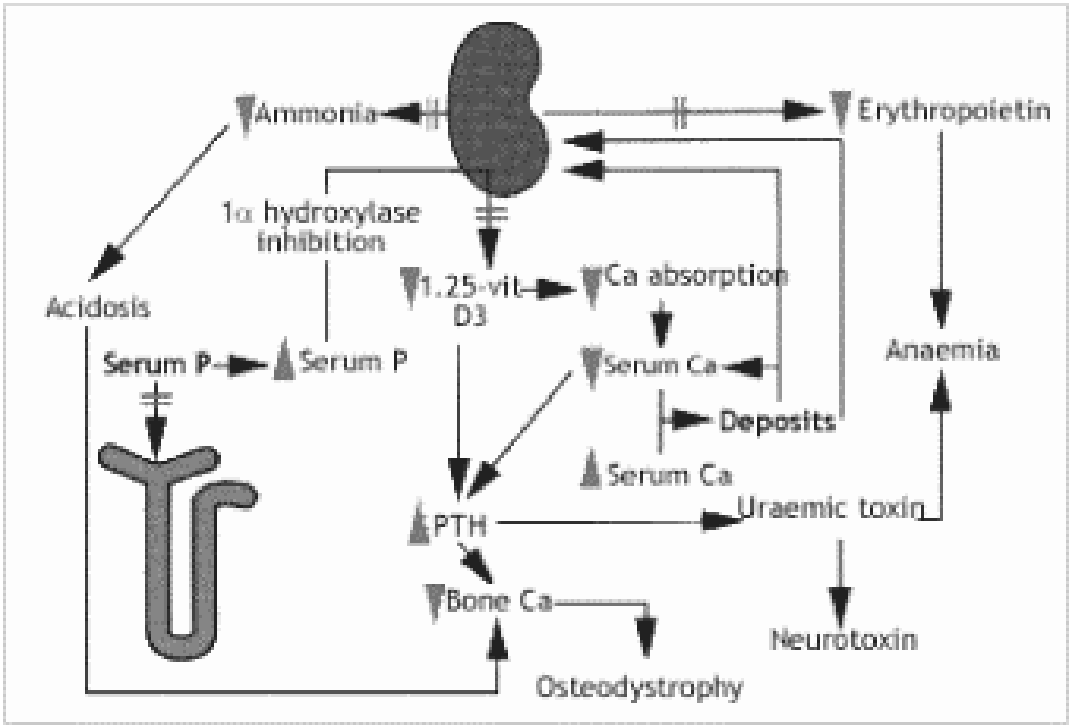


TABLE - A

VARIATIONS IN THYROID HORMONES AND BINDING PROTEIN IN HYPER AND HYPOTHYROIDISM

Condition	**Concentrations of Binding Proteins**	**Total Plasma T_4, T_3, rT_3**	**Free Plasma T_4, T_3, rT_3**	**Plasma TSH**	**Clinical State**
Hyperthyroidism	Normal	High	High	Low	Hyperthyroid
Hypothyroidism	Normal	Low	Low	High	Hypothyroid

CHRONIC RENAL FAILURE MANIFESTATION



MASTER CHART

Sl. No.	Name	Age yrs	Sex	I.P.No.	Symptoms Duration	Cholestral mg/dl	Renal parameters			Thyroid Profile			USG Abdomen	Miscelaneous
							Ureamg/dl	Creatinine mg/dl	Creatinine clearance ml/min	T3 ng/ml	T4 μg/dl	TGH μlU/ml		
1.	Munusamy	54	M	020271	5 months	171	88	4.6	19	0.5	3.2	2.3	BLCK	1
2.	Harikrishnan	47	M	062294	24 months	230	103	10.4	8	0.5	5.3	4.5	BLCK	1
3.	Namasivayam	30	M	020434	4 months	164	130	8.5	9	0.5	3.2	2.3	BLCK	1
4.	Mariyappan	64	M	062483	8 months	280	96	4.6	19	1	7.3	7	BLCK	2
5.	Nagammal	52	F	6314	7 months	171	79	4.4	19	2	7.3	2.1	BLCK	1
6.	Ismail	56	M	062517	5 months	160	150	6.2	12	1	4.9	6.5	BLCK	1
7.	Nagaiay	59	M	010038	9 months	180	107	4.6	16	0.2	7.9	3.6	BLCK	NIL
8.	Jeyalakshmi	66	F	009978	10 months	110	120	8.5	8	0.2	0.5	27	BLCK	1
9.	Kumar	47	M	062367	6 months	171	124	8.2	9	0.3	3.2	3.1	BLCK	1
10.	Krishnan	27	M	008903	5 months	198	70	5.4	12	0.2	3	10	BLCK	1
11.	Sumathy	48	F	061957	7 months	162	84	3.5	17	1	8.1	1.1	BLCK	1
12.	Lakshmi	63	F	061871	36 months	181	140	16	6	0.2	4.6	1.5	BLCK	1
13.	Rajendran	45	M	062532	9 months	172	87	2.6	34	1.2	8.2	10.5	BLCK	1
14.	Arokiyada	52	M	062373	7 months	190	170	16.4	6	0.2	4.5	2.8	BLCK	1
15.	Gopal	52	M	013547	5 months	184	163	13.6	7	0.2	1.7	7.6	BLCK	3
16.	Kumar	47	M	014428	7 months	190	136	12	8	0.2	8.5	4.5	BLCK	1
17.	Gopirao	27	M	70656	12 months	192	96	5.4	10	0.7	5.5	0.7	CMDL	1

Sl. No.	Name	Age yrs	Sex	I.P.No.	Symptoms Duration	Cholestral mg/dl	Renal parameters			Thyroid Profile			USG Abdomen	Miscelaneous
							Ureamg/dl	Creatinine mg/dl	Creatinine clearance ml/min	T3 ng/ml	T4 µg/dl	TGH µlU/ml		
18.	Indrani	49	F	013823	8 months	185	64	3.2	16	0.4	5.8	3.5	BLCK	4
19.	Chinnaraja	53	M	062738	12 months	190	82	2.8	31	1.1	7.9	2.3	BLCK	1
20.	Rajeswari	62	F	011469	5 months	160	120	12.8	7	0.4	2.8	25	BLCK	1
21.	Ismal	51	M	062968	9 months	184	77	3.4	17	0.7	6.4	1	CMDL	NIL
22.	Amirthammal	55	M	011456	24 months	175	135	11.8	8	1.3	5.5	5.8	BLCK	1
23.	Murugesh	24	M	062571	6 months	160	68	2.4	22	0.9	6.1	0.7	BLCK	NIL
24.	Mannavalan	77	M	014987	5 months	180	84	3.4	17	0.9	5.4	4.6	BLCK	NIL
25.	Sakthevelu	23	M	61214	7 months	176	82	5.4	10	0.7	6.2	2.1	BLCK	1
26.	Ravichandran	45	M	62075	24 months	270	80	3.2	16	1	5.2	6.5	BLCK	NIL
27.	Kollappan	67	M	063130	5 years	220	170	14.7	7	0.2	2.2	13.5	BLCK	3
28.	Rajendran	42	M	063883	7 months	210	72	2.4	22	1.1	5.6	7	BLCK	5
29.	Palanisamy	54	M	016627	5 months	186	82	3.2	16	0.4	8.9	2.1	BLCK	2
30.	Mukandiah	29	M	70720	7 months	150	128	12	7	0.75	6.5	3.7	BLCK	1
31.	Ramalingam	56	M	020715	4 months	184	77	3.4	17	0.7	6.4	1	BLCK	NIL
32.	Kumar	47	M	063756	7 months	217	90	5.6	10	0.5	5	4.5	BLCK	1
33.	Rajendran	43	M	063600	7 months	133	68	2.4	22	0.9	6.1	0.7	CMDL	NIL
34.	Maraghadam	52	F	062655	5 months	296	104	5	17	0.5	2.5	23	BLCK	1
35.	Asokan	27	M	70598	9 months	168	74	2.6	34	0.7	6.2	2.1	BLCK	2
36.	Chinnathambi	47	M	063245	36 months	203	100	13.5	8	1.4	7.8	12.5	BLCK	1

Sl. No.	Name	Age yrs	Sex	I.P.No.	Symptoms Duration	Cholestral mg/dl	Renal parameters			Thyroid Profile			USG Abdomen	Miscelaneous
							Ureamg/dl	Creatinine mg/dl	Creatinine clearance ml/min	T3 ng/ml	T4 µg/dl	TGH µlU/ml		
37.	Mohan	30	M	062650	36 months	184	170	14.7	7	0.2	2.2	23	BLCK	1
38.	Ambigai Raj	68	M	063279	24 months	164	148	8.4	8	0.2	7.4	2	BLCK	1
39.	Premraj	54	M	015799	7 months	186	82	4.6	19	0.4	8.9	2.1	CMDL	2
40.	Nallamuthu	53	M	016546	4 months	133	123	7.6	10	0.4	2.2	5	CMDL	1
41.	Kumar	44	M	063086	9 months	146	98	5.1	12	0.8	6.3	1.7	BLCK	NIL
42.	Sankar	48	M	017109	7 months	168	70	2.3	34	0.5	2.2	5	BLCK	1
43.	Noormohamed	30	M	063376	5 months	174	122	5.4	11	0.3	3.2	24.5	BLCK	1
44.	Kuppammal	43	F	014249	7 months	273	92	5.1	12	1	8.8	0.6	BLCK	1
45.	Indrani	48	F	63152	4 months	164	76	3.2	16	0.5	7.2	5.1	BLCK	1
46.	Yakob	64	M	016533	8 months	196	78	4.8	15	0.8	9.5	7	BLCK	2
47.	Murugesh	26	M	063122	7 months	156	82	2.3	34	0.4	5.5	13.5	BLCK	2
48.	Pandian	42	M	063843	5 months	162	78	4.6	34	0.7	9.2	2.7	BLCK	1
49.	C. Mani	56	M	064114	12 months	171	124	6.3	10	0.5	6.2	12.7	BLCK	1
50.	Nallamuthu	52	M	019178	10 months	181	73	2.4	21	1.9	6.9	2.9	BLCK	1

1 - Hypothyroid symptom Present
2 - Delayed Ankle Jerk
3 - Papilledema
4 - Goiter
5 - Pleural Effusion Present

BLCK - Bilateral Contracted Kidney
CMDL - Cortico Medullary Differentiation Lost